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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/677,701	10/02/2003	Victor V. Levenson	NWESTERN-08390	9778

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EXAMINER	
GOLDBERG, JEANINE ANNE	
ART UNIT	**PAPER NUMBER**
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/677,701	LEVENSON ET AL.	
	Examiner	Art Unit	
	Jeanine A. Goldberg	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14, 23-31, 33* is/are pending in the application.

4a) Of the above claim(s) *30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14,23-29, 31 and 33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to the papers filed September 10, 2007. Currently, claims 1-14, 23-31, 33 are pending.

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 18, 2007 has been entered.

3. Any rejections not re-iterated herein are hereby withdrawn.

Election/Restrictions

4. In view of the amendments to the claims to require DAPK and PR, a particular combination, the claims have been examined on the merits.

5. Claims 30 are drawn to combinations of promoters not previously elected. In the event that the generic claim becomes allowable, the combinations comprising at least 40 genes would be rejoined.

Priority

6. This application claims priority to provisional 60/415,628, filed October 2, 2002.

Drawings

7. The drawings are acceptable.

Claim Rejections - 35 USC § 112-Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 3-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for detecting methylation in DAPK and PR genes, does not reasonably provide enablement for characterizing cancer based upon methylation profiles for DAPK and PR. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the

relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention and breadth of claims

Claims 3-14 are drawn to method of characterizing cancer by providing a sample from a subject diagnosed with breast cancer and detecting the presence or absence of DNA methylation in DAPK and PR. The invention is in a class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The unpredictability of the art and the state of the prior art

Maat et al. (Investigative Ophthalmology, Visual Science, Vol 48, No. 2, pages 486-490, February 2007) teaches a positive correlation was found between RASSF1a promoter methylation and development of metastatic disease, however a correlation with disease-free survival could not be established (abstract). Furthermore, Maat teaches that high frequency of RASSF1A methylation in cell lines compared with primary tumors was observed. Maat also teaches p16 methylation was more common in cell lines than tumors (page 489, col. 2). Thus Maat teaches that promoter methylation in genes is not indicative of any characterization and further that cell lines are not reliable predictors of tumor methylation.

Henrique et al. (Clin Cancer Research, Vol. 13, No. 20, pages 6122-6129, October 2007) teaches methylation patterns of different genes are associated with different characterizing events. For example, APC methylation appears to be associated with clinical Gleason score, however, CCND2, RARB2 are not associated with Gleason score. Henrique further teaches that APC hypermethylation was not significantly found to be associated with disease specific survival (page 6127, col. 1).

Moreover, Henrique teaches that from a panel of five genes, CCND2 did not show a significant association with disease-free survival in a univariate analysis (page 6128, col.2).

Suzuki et al. (Cancer Letters, Vol. 242, pages 222-230, 2006) teaches methylation patterns in cancer and finds that aberrant methyylation differed between genes (see Table 4). Moreover, as seen in Figure 2, when analyzed in comparison to stages, different genes were found to have different patterns. Only one gene was significantly associated, namely CRBP1. Further, RIZ1 showed an inverse relationship from all the other genes. Thus it is unpredictable, with out experimentation that is unpredictable whether genes are associated with stages or GS, for example.

Chang et al. (J. Mol. Med, Vol. 83, pages 132-139, 2005) teaches tamoxifen-resistant breast cancers show less frequent methylation of the estrogen receptor B but not the estrogen receptor alpha gene. Chang teaches that the methylation of ERB but not eh ERA was associated (abstract and Table 2). Thus, each gene is not similarly associated with resistance to drugs.

Maruya et al. (Clinical Cancer Research, Vol. 10, pages 3825-3830, June 2004) teaches cell lines and primary were analyzed and there was variability within and between cell lines and tumor specimens. This supports a heterogeneous and dynamic state of methylation in genes (abstract). Maruya clearly states that cell lines and carcinoma specimens manifest variable levels of methylation (page 3928, col. 2).

House (J. Gastrointest Surg, Vol. 7, pages 1004-1014, 2003) teaches analysis of promoter methylation in numerous genes. House teaches that statistical significance was reached only for tumor necrosis and E-cadherin gene methylation. Further, only E-cadherin methylation and absence of hMLH1 methylation correlated with early tumor recurrence. House analyzed the survival disadvantage at 5 years and found that the

promoter status of 10 tumor suppressor genes were not significant as prognostic markers (page 1009, col. 1-2).

Guidance in the Specification.

The specification teaches methylation profiling in lymphoma cell lines (Figure 7). DAPK and PR are illustrated. For DAPK, 0% of the 8 controls have methylation while 33% of the T-cell lines were methylated. Similarly, for PR, 0% of the 8 control samples have methylation while 50% of the T-cell lines were methylated.

Table 1, page 76, illustrates differences between two cell lines. For example DAPK, was methlated in MCF7, but not methylated in T47D wt. Thus, cell lines do not appear to consistently demonstrate methylation.

The specification detects methylation in MDA-MD-231 breast cancer cell lines treated with 5-aza-2' deoxycytidine (page 77). The specification teaches analysis of 10 samples from patients. The specification fails to provide any results of the analysis, in particular with respect to DAPK or PR.

Figure 2 illustrates the methylation of 40 promoters in breast tumor tissue and normal breast tissue. As seen, the methylation of DAPK is unpredictable. DAPK is methylated in 5/5 normal tissues and in 4/5 breast tumor tissues (page 79). Moreover, PR is similarly methylated unpredictable.

The guidance provided by the specification amounts to an invitation for the skilled artisan to try and follow the disclosed instructions to make and use the claimed invention.

Working Examples

The specification has no working examples of characterizing cancer for detecting chemotherapy resistant cancer, chance of disease free survival, risk of developing metastatic disease, monitoring progression.

Quantity of Experimentation

The quantity of experimentation in this area is extremely large since there is significant number of parameters which would have to be studied.

The specification and the art clearly illustrate the unpredictability of cell lines and the differences in methylation. It is unpredictable given the small sample size with lack of significance whether any association between DAPK and PR exist without further experimentation. Maat teaches that high frequency of RASSF1A methylation in cell lines compared with primary tumors was observed. Maat also teaches p16 methylation was more common in cell lines than tumors (page 489, col. 2). Thus Maat teaches that promoter methylation in cell lines are not reliable predictors of tumor methylation. Similarly, Maruya teaches cell lines and primary were analyzed and there was variability within and between cell lines and tumor specimens. This supports a heterogeneous and dynamic state of methylation in genes (abstract). Maruya clearly states that cell lines and carcinoma specimens manifest variable levels of methylation (page 3928, col. 2). Thus, analysis of cell lines without further experimentation in tumor cell lines would require unpredictable analysis regarding association of methylation patterns in tumor cells.

Claim 5 is specifically directed to detecting the presence or absence of chemotherapy resistant cancer. The specification fails to provide any guidance of how to characterize the cancer in such a manner. The art clearly teaches that different genes are differentially associated with resistance. Specifically, Chang teaches

tamoxifen-resistant breast cancers show less frequent methylation of the estrogen receptor B but not the estrogen receptor alpha gene. Chang teaches that the methylation of ERB but not the ERA was associated (abstract and Table 2). Thus, each gene is not similarly associated with resistance to drugs. It would be unpredictable whether DAPK and PR are associated with chemotherapy resistant cancer because the state of the art teaches that without unpredictable and undue experimentation, different genes methylation patterns vary with respect to the association with resistance.

Claim 7 is specifically directed to detecting a chance of disease-free survival, metastatic disease and progression. The specification fails to provide any guidance of how to characterize the cancer in such a manner. The art clearly teaches that different genes are differentially associated with disease-free survival, metastatic disease and progression. The art teaches numerous situations where methylation patterns could not be established to be associated with a chance of disease-free survival, metastatic disease and progression. For example, Maat teaches a positive correlation was found between RASSF1a promoter methylation and development of metastatic disease, however a correlation with disease-free survival could not be established (abstract). Moreover, House teaches analysis of promoter methylation in numerous genes. House teaches that statistical significance was reached only for tumor necrosis and E-cadherin gene methylation. Further, only E-cadherin methylation and absence of hMLH1 methylation correlated with early tumor recurrence. House analyzed the survival disadvantage at 5 years and found that the promoter status of 10 tumor suppressor genes were not significant as prognostic markers (page 1009, col. 1-2). Therefore, for each particular gene and each particular "characterization" of disease-free survival, metastatic disease and progression, individual experimentation which is unpredictable

and undue would be required. The experimentation would be trial and error experimentation with no expectation of success. This would require significant inventive effort, with each of the many intervening steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps.

Level of Skill in the Art

The level of skill in the art is deemed to be high.

Conclusion

In the instant case, as discussed above, in a highly unpredictable art where the art teaches the lack of association between genes and different characterizations including disease-free survival, metastatic disease and progression, the broad scope of the claims would require significant unpredictable and undue experimentation. Further, the prior art and the specification provides insufficient guidance to overcome the art recognized difficulties. Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the absence of a working example and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1-2, 23-24, 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kusui et al. (Biochemical and Biophysical Research Communications, Vol. 289, pages 681-686, 2001) in view of Yan et al. (Clinical Cancer Research, Vol. 6, pages 1432-1438, April 2000), Wong (Cancer Research, Vol. 39, pages 71-73, 1999) and Broude et al. (PNAS, Vol. 98, No. 1, pages 206-211, January 2001).

Kusui teaches analysis of DNA methylation of the human oxytocin receptor gene promoter that regulated tissue specific gene suppression. Kusui teaches digesting genomic DNA with methylation sensitive restriction enzyme HpaII and amplifying the

promoter with gene specific primers.. Kusui specifically teaches peripheral blood was obtained from humans. Genomic DNA was extracted from tissues and digested with BamHI and HpaII which are both methylation sensitive enzymes. The digested DNA was analyzed by PCR using primers specific for the OTR gene (page 683, col. 1). Kusui specifically teaches that after the complete digestion of the genomic DNA, fragments were amplified with PCR (page 684, col. 2)(limitations of Claim 31).

Kusui does not specifically teach analysis of a plurality of promoters with 5 pairs of gene –specific primers in a plasma sample.

However, Yan et al. teaches Cpg Island arrays for deciphering epigenetic signatures of breast cancer. Yan teaches an array based method for differential methylation hybridization (DMH) which allows for genome-wide screening of Cpg island hypermethlation. Yan specifically teaches obtaining patient samples from female patients undergoing mastectomies to isolate high molecular weight DNA (limitations of Claim 21, 24). Yan further teaches analyzing genomic DNA that was digested and amplified (page 1433, col.1). Yan teaches performing array hybridization on nylon membranes (page 1433, col. 2). Yan teaches normal and tumor amplicons were analyzed (limitations of Claim 2). As seen in Figure 1, the results of DMH are illustrated. CpG island tags were arrayed for secondary DMH screening in the patient group. Yan teaches the array based method allows semiquantification of the methylation differences, hybridization signal intensity. Moreover, Yan teaches the benefits of DMH such that high-throughput microarray based assays allow for detection of many CpG island hypermethylation at the whole genome level.

Moreover, Wong teaches analysis of methylation in the plasma and serum of cancer patients. Wong teaches the method of analysis is noninvasive detection of a wide variety of cancers.

Further, Broude et al teaches multiplex amplification provides simultaneous amplification of many targets of interest in one reaction thus increasing the assay throughput and allowing more efficient use of each DNA sample. Broude teaches the use of gene specific primers in combination to amplify multiple targets. Broude teaches three parameters are important in evaluating the quality of multiplex amplification reactions including uniformity of amplification of different targets, the amount of primer dimmers and the non-specific background or signal to background ratio (page 208, col. 2).

Therefore, it would have been prima facie obvious at the time the invention was made to have performed the method of Kusui to detect methylation in promoter regions of known genes and improved the detection method using the array based analysis of Yan in serum as taught by Wong and used multiple gene specific primers for high throughput analysis. Kusui specifically teaches obtaining amplicons from methylated nucleic acids using gene specific primers. Moreover, Broude teaches that multiplex analysis of multiple targets using gene specific primers may be performed in a single reaciont to increase throughput and allow more efficient use of a DNA sample. The ordinary artisan would have been motivated to have generated a high-throughput analysis of the amplicons on an array, as taught by Yan to obtain the expected benefits of analysis of numerous nucleic acids simultaneously and allow detection at the whole

genome level. Thus, analyzing the amplicons generated by Kusui on an array taught by Yan would have been obvious at the time the invention was made for the specific benefits of high-throughput taught by Yan. Moreover, the ordinary artisan would have been motivated to have used a plasma sample because Wong teaches methylation may be analyzed in a plasma sample which is a noninvasive method for obtaining a sample.

11. Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kusui et al. (Biochemical and Biophysical Research Communications, Vol. 289, pages 681-686, 2001) in view of Yan et al. (Clinical Cancer Research, Vol. 6, pages 1432-1438, April 2000) and Wong (Cancer Research, Vol. 39, pages 71-73, 1999) and Broude et al. (PNAS, Vol. 98, No. 1, pages 206-211, January 2001) as applied to Claims 1-2, 21, 23-24, 31 above and further in view of Huang (US Pat. 6,605,432, August 12, 2003).

Neither Kusui, nor Yan, specifically teach using the Hin6I methylation sensitive enzyme for digesting.

However, Huang teaches analysis of high throughput methods for detecting DNA methylation. Huang teaches after amplification, methylation-sensitive sites of the amplified products are preferably identified by digestion with a methylation-sensitive restriction enzyme. Examples of such methylation-sensitive enzymes are BstU I, SmaI, SacII, EagI, MspI, HpaII, HhaI and BssHII which digest non-methylated CpG dinucleotide regions (limitations of Claim 14). Positive CpG dinucleotide nucleic acid fragments containing the methylation-sensitive sites are used for DMH analysis.

Therefore it would have been prima facie obvious to the skilled artisan at the time the invention was made to modify the method of Kusui, and Yan, to digest with Hin6I, an equivalent methylation sensitive enzyme. Kusui teaches digesting with HpaII. Huang teaches that BstUI and HhaI (also known as Hin6I) are methylation sensitive enzymes for digesting and analysis of methylation patterns.

12. Claims 26-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kusui et al. (Biochemical and Biophysical Research Communications, Vol. 289, pages 681-686, 2001) in view of Yan et al. (Clinical Cancer Research, Vol. 6, pages 1432-1438, April 2000), Wong (Cancer Research, Vol. 39, pages 71-73, 1999) and Broude et al. (PNAS, Vol. 98, No. 1, pages 206-211, January 2001) as applied to Claims 1-2, 23-24, 31 above and further in view of Pogribny et al. (Biochemical and Biophysical Research Communications, Vol. 262, pages 624-628, 1999).

Kusui nor Yan nor Wong not Broude et al teaches using two aliquots and digesting one aliquot for control analysis.

However, Pogribny teaches analysis of methylation patterns in DNA which includes detecting sequence specific alterations in DNA methylation. Pogribny specifically teaches using a DNA aliquot and digesting it overnight with HpaII or BssHII. Then in a second DNA aliquot no restriction enzyme is added. This serves as background control. The single nucleotide reaction is then performed on the aliquots.

Therefore, it would have been prima facie obvious at the time the invention was made to have performed the method of Kusui to detect methylation in promoter regions

of known genes and improved the detection method using the array based analysis of Yan in serum as taught by Wong and used multiple gene specific primers for high throughput analysis and include a control assay which does not digest with a methylation sensitive enzyme for background control. The ordinary artisan would have been motivated to have controlled for background using the two aliquot method of Pogribny.

13. Claim 33 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kusui et al. (Biochemical and Biophysical Research Communications, Vol. 289, pages 681-686, 2001) in view of Yan et al. (Clinical Cancer Research, Vol. 6, pages 1432-1438, April 2000), and Broude et al. (PNAS, Vol. 98, No. 1, pages 206-211, January 2001) as applied to Claims 1-2, 23-24, 31 above and further in view of Pogribny et al. (Biochemical and Biophysical Research Communications, Vol. 262, pages 624-628, 1999).

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Kusui specifically teaches that after the complete digestion of the genomic DNA, fragments were amplified with PCR (page 684, col. 2)(limitations of Claim 31).

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Further, Broude et al teaches multiplex amplification provides simultaneous amplification of many targets of interest in one reaction thus increasing the assay throughput and allowing more efficient use of each DNA sample. Broude teaches the use of gene specific primers in combination to amplify multiple targets. Broude teaches

three parameters are important in evaluating the quality of multiplex amplification reactions including uniformity of amplification of different targets, the amount of primer dimmers and the non-specific background or signal to background ratio (page 208, col. 2).

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Therefore, it would have been prima facie obvious at the time the invention was made to have performed the method of Kusui to detect methylation in promoter regions of known genes and improved the detection method using the array based analysis of Yan and used multiple gene specific primers for high throughput analysis and include a control assay which does not digest with a methylation sensitive enzyme for background control. Kusui specifically teaches obtaining amplicons from methylated nucleic acids using gene specific primers. Moreover, Broude teaches that multiplex analysis of multiple targets using gene specific primers may be performed in a single reaction to increase throughput and allow more efficient use of a DNA sample. The ordinary artisan would have been motivated to have generated a high-throughput analysis of the amplicons on an array, as taught by Yan to obtain the expected benefits of analysis of numerous nucleic acids simultaneously and allow detection at the whole genome level. Thus, analyzing the amplicons generated by Kusui on an array taught by Yan would

have been obvious at the time the invention was made for the specific benefits of high-throughput taught by Yan. Moreover, the ordinary artisan would have been motivated to have used a plasma sample because Wong teaches methylation may be analyzed in a plasma sample which is a noninvasive method for obtaining a sample.

Conclusion

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (571) 272-0743. The examiner can normally be reached Monday-Friday from 7:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571) 272-0735.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

The Central Fax Number for official correspondence is (571) 273-8300.

J. Goldberg

Jeanine Goldberg
Primary Examiner
November 26, 2007